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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,967	06/19/2000	Bertil Abrahamsson	1103326-0624	6706

7590 02/22/2002

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EXAMINER
YOUNG, MICAH PAUL

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,967	ABRAHAMSSON ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10,15-19,22 and 24-27 is/are pending in the application.

4a) Of the above claim(s) 22 and 27 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10,15-19 and 24-26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 22 and 27, drawn to a method of treating diarrhea with an IBAT inhibitor, classified in class 424, subclass 400.

   II. Claims 1-10, 15-19 and 24-26, drawn to a formulation comprising an IBAT inhibitor and a carrier, and a method for treating hypercholesterolemia, classified in class 424, subclass 78.1.

The inventions are distinct, each from the other because:

2. The processes disclosed are capable of supporting separate patents. The process of group I is to the treatment of diarrhea during while the process of group II is to a treatment of hypercholesterolemia. Also, the classification of these two groups is different and would incur an undo search on the examiner.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. A telephone call was made to John Genova on February 12, 2002 to request an oral election to the above restriction requirement, and an election of group II was made.

The prosecution of the remaining claims is as follows:

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-10, 15-19 and 24-26 are all rejected under 35 U.S.C. 103(a) as being unpatentable over Brieaddy et al (USPN 5723458) in view of Hirakawa et al (USPN 5614220) and Spielvogel et al (USPN 5659027). Claims 1-10, 16-19 and 24 are all drawn to an oral formulation comprising an IBAT inhibitor and a pharmaceutically acceptable carrier. Claims 1-10 and 24 recite that the formulation along with its components (carrier and IBAT inhibitor) are released at specific regions of the intestinal tract, the proximal ileum. The claims also provide a lag-time of about 0.5-2 hours after the emptying the stomach. Also, the claims further recite that the formulation is triggered by the pH difference between the jejunum and the ileum.

Claims 16-19 further describe the formulation as being formulated for simultaneous, separate or sequential administration of the medicament. The claims further recite that the

formulation comprises a bile acid binder along with the IBAT inhibitor, and that this binder is to be released in the colon.

Brieaddy et al (USPN 5723458) teaches a hypolipidaemic compound attached to a carrier. The reference teaches that the compound is sufficient in the inhibition of bile acid uptake (Abstract; column 9, lines 37-52). The reference does not teach the specific release locations as recited by the claims.

Spielvogel et al (USPN 5659027) teaches a boron-based hypolipidaemic compound attached to a carrier. The reference teaches that the compound can be attached to a bile acid binder colestipol (column 8, lines 40-58). The reference also teaches that the compound was tested in the ileum and colon for hypolipidaemic activity (Table 2). Though the reference does teach the treatment of intestinal ailments, it does not teach the delivery mechanism required.

Hirakawa et al (USPN 5614220) teaches a pharmaceutical preparation specifically targeted for the intestinal tract (Abstract). The reference suggests that medical active ingredients such as "agents affecting digestive organs" (column 4, lines 29-31). The formulation also is a delayed release formulation with a lag-time of at least 2 hours and is triggered by a change of pH (column 4, lines 5-15; column 5-6, lines 64-14). Though the reference does not specifically teach a hypolipidaemic compound in use with the formulation, or the same targeting location in the intestinal tract, the suggestion of organ affecting drugs along with the teachings of the pH release of the medicine.

One of ordinary skill in the art would have been motivated to combine the either the compounds of Brieaddy or Spielvogel with the formulation of Hirakawa in order to inhibit bile uptake in the intestinal tract, specifically the ileum and colon. Though these teachings do not

teach the specific release locations of the claimed invention (proximal ileum, distal jejunum) the general area is understood and taught by the reference. The release of the medicament due to a change in pH is taught by Hirakawa and would be obvious to one of ordinary skill in the art to modify it to release a medicament between any pH gradient. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955). It would have been obvious to one of ordinary skill in the art, at the time of the invention to combine these teachings with the expected result of a hypolipidaemic formulation useful in the uptake of bile acid in the intestinal tract with specific activity in the ileum and distal jejunum.

Claims 15, 25-26 are drawn to methods of preparations of the formulation of claims 1-10 and for the treatment of hypercholesterolemia with the formulation. Brieaddy et al provides methods for both the preparation of a hypolipidaemic compound and a treatment of hypercholesterolemia using the compound (column 8, lines 40-46; column 8, lines 53-60). The reference is only deficient as is stated above, and can be substituted into the formulation of Hirakawa to fulfill the limitations of the claimed invention. One of ordinary skill in the art would have been motivated to combine the teachings of Brieaddy with those of Hirakawa due to the inhibit bile uptake and treat hypercholesterolemia. It would have been obvious to one of ordinary skill in the art, at the time of the invention to combine these teachings with the expected result of a hypolipidaemic formulation useful in the uptake of bile acid, and a method for the treatment of high cholesterol. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am-4: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-5014.

Micah-Paul Young
Examiner
Art Unit 1615

MPY
February 19, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600